280-120

GP184
31
1073

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on November 21, 1994.
(Date of Deposit)

By _____ 12-16-94

CGNE 62-1(1)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of	
Comai, *et al.*	Examiner: P. Moody
Serial No. 07/985,742	Art Unit: 1804
Filed: December 4, 1992	APPEAL BRIEF UNDER 37 C.F.R. §1.192
For: FIGWORT PLANT PROMOTER AND USES	

Honorable Commissioner of
Patents and Trademarks
Washington, DC 20231

Dear Sir:

Applicants submit this brief, in triplicate, in support of an Appeal to the Board of Patent Appeals and Interferences from the decision of the Patent Office in a final action dated January 24, 1994, wherein all claims in the above application were rejected. The claims under appeal are found in the accompanying Appendix.

STATUS OF CLAIMS

Claims 20, 22-28, 30, 33-36 and 43 remain pending and are under appeal.

STATUS OF AMENDMENTS

In the January 24, 1994, Final Office Action, it was indicated that amendments made in Applicants' response dated November 10, 1993, were entered. For the purpose of better presenting the claims and narrowing the issues for appeal, Applicants submit an amendment herewith which returns Claim 20 to its form prior to the November 10, 1993, amendment. Upon entrance of the accompanying amendment, the claims under appeal will be those contained in the appendix to this appeal.

SUMMARY OF THE INVENTION

Applicants claim a recombinant construct which comprises the 34S promoter developed from the Figwort Mosaic Virus (FMV). The 34S promoter is a promoter analogous to the 35S promoter of cauliflower mosaic virus (CaMV), in being constitutively active, a strong promoter of transcription and not notably organ specific.

More particularly, Applicants took various segments of DNA from the genome of figwort mosaic virus (FMV) strain M3, tested them, and discovered a region which possessed strong promoter activity. This promoter of FMV is divergent in sequence with, but has promoter activity equivalent to that of, the 35S promoter from CaMV. As the 35S promoter is named for the sedimentation coefficient of its product, *i.e.*, the genome-length RNA transcript, and the FMV genome is slightly

smaller than that of CaMV, Applicants designated this FMV promoter as the "34S promoter".

ISSUES

Issue 1

Whether Claims 20, 22-27 and 33-35 are patentable under 35 U.S.C. §102(a) in view of Gowda *et al.* or Wu *et al.*, or whether the §1.131 declaration submitted in prosecution overcomes these references.

Issue 2

Whether the rejection of Claims 20, 22-27 and 33-36 under §102(a) in view of Goldberg *et al.* should stand, or whether this rejection is overcome by the §1.131 declaration from Comai *et al.* submitted in prosecution.

Issue 3

Whether under 35 U.S.C. §103 Claims 20, 22-28, 30, 33-36 and 43 are patentable over Shah *et al.* and Sanders *et al.* taken with Richins *et al.* or Gowda *et al.*, or Wu *et al.* or Goldberg *et al.*.

Issue 4

Whether Claims 20, 22-28, 30, 33-36 and 43 are patentable under 35 U.S.C. §103 in view Shah *et al.* and Sanders *et al.* taken with Richins *et al.* and Shepherd *et al.*.

GROUPING OF THE CLAIMS

Issue 1

Only Claims 20, 22-27 and 33-35 are rejected for purposes of Issue 1.

Issue 2

Only Claims 20, 22-27 and 33-36 are rejected under Issue 2.

Issue 3

The claims under appeal form a single grouping with regard to Issue 3.

Issue 4

The claims under appeal are grouped together for purposes of Issue 4.

ARGUMENT

Issue 1

Claims 20, 22-27 and 33-35 are rejected under 35 U.S.C. §102(a) in view of Gowda *et al.* or Wu *et al.*.

Applicants had earlier submitted a declaration under §1.131 that removed this rejection, however, the rejection was reinstated in an Office Action dated May 28, 1993 (see page 2 of that Office Action). The rejection was reinstated by the Patent Office when a review of the file indicated that the first submitted §1.131 declaration was signed only by Dr.

Sanger. This first declaration was accepted by the Patent Office in an Office Action dated March 19, 1992, (see page 5 of that Office Action), in response to an amendment canceling certain claims and adding, among others, Claims 20 and 36 (Applicants response dated November 21, 1991).

In their November 10, 1993 response Applicants submitted a new §1.131 declaration signed by all of the inventors, demonstrating completion of the invention prior to November 13, 1988. This declaration is very nearly identical (but for originating from all three inventors) to the declaration which was previously accepted by the Patent Office as removing the references forming the §102(a) rejections. While this indication (November 21, 1991 Office Action) was specifically with regard to Claims 1-11 and 16-17, now canceled, in that same Office Action claims 20-42 were pending.

In the Final Office Action dated January 24, 1994, the rejection was reinstated for the given reason that the previously submitted §1.131 declaration which had removed these §102(a) references does not show possession of the claimed invention, in not mentioning plants and in failing to mention constitutive transcription. Applicants presume that the differential treatment given these nearly identical declarations has to do with the subject matter added by amendment to Claim 20 in Applicants' response dated November 10, 1993 (Claim 20 as presented in the amendment accompanying

this appeal brief has been amended to no longer recite constitutive plant expression).

Since the Patent Office accepted this declaration previously as overcoming this rejection, it is believed that the claims, as presently amended, claim an invention which is clearly shown to have been in the possession of the inventors in the work with is the recounted in the declaration. In any case, Applicants note that original Claim 17 recited a plant containing a construct, and that the type of expression, constitutive or otherwise, provided by the claimed 34S promoter is an inherent feature of the invention.

As the declaration removes the Gowda *et al.* and Wu *et al.* references as prior art against the invention as claimed, Applicants respectfully request the reversal of the §102(a) rejection.

Issue 2

The Patent Office has similarly maintained the reinstated rejection of Claims 20, 22-27 and 33-36 under §102(a) in view of Goldberg *et al.*, for the same reasons given above with respect to the Gowda *et al.* and Wu *et al.* references.

For the same reason as given above, that the Comai *et al.* declaration provided during prosecution clearly should act to remove the Gowda *et al.* reference as prior art with regard to the claims as presented for appeal (see November

21, 1994 amendment), and Applicants respectfully request the reversal of the §102(a) rejection over Goldberg *et al.*.

Issue 3

Claims 20, 22-28, 30, 33-36 and 43 are rejected under 35 U.S.C. § 103 over Shah *et al.* and Sanders *et al.* taken with Richins *et al.* or Gowda *et al.*, or Wu *et al.* or Goldberg *et al.*.

As to the Gowda *et al.*, Wu *et al.* and Goldberg *et al.* secondary references, as previously discussed with regard to Issues 1 and 2, the Comai *et al.* declaration removes these secondary references as prior art with respect to the claims as amended.

Shah *et al.* describes DNA constructs for expression using Cauliflower Mosaic Virus (CaMV) 35S promoters. The other primary reference, Sanders *et al.*, compares the strength of CaMV 35S and nopaline synthase (nos) promoters in leaves from transgenic plants, teaching that higher levels of expression are possible using the 35S promoter.

The Patent Office states that these primary references disclose all features of Applicants' invention except for specifying the FMV 34S promoter as an alternative viral promoter to the 35S promoter of CaMV, which is presumed from Richins *et al.*.

While Shah *et al.* teaches the use of the 35S promoter of CaMV, this knowledge of the 35S promoter of CaMV, even coupled with the general knowledge of plant promoters which

was available at the time of the invention, was not sufficient to provide the skilled artisan with the FMV plant promoter given only the FMV genomic sequence disclosed in by Richins *et al.*.

A § 103 rejection requires consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in art that they should make claimed invention, and 2) whether the primary art would also have revealed that in so making or carrying out the invention a person of ordinary skill would have a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991) (*citing In re Dow Chemical Co.*, 837 F.2d 469, 437 (Fed. Cir. 1988)). Both the suggestion and reasonable expectation of success must be founded in the prior art, not in applicant's disclosure. *Id.*

Nothing in the prior art identified the 34S promoter of FMV as a known alternative promoter to the 35S promoter of CaMV. In fact, no reference taught or disclosed any promoter of FMV as a known promoter, let alone an acceptable alternative to the CaMV 35S promoter. There is no teaching or suggestion in the primary or secondary references that CaMV 35S-like levels of expression may be obtained with any FMV promoter.

Richins *et al.*, discloses only the genomic sequence to FMV, <u>not</u> the FMV 34S promoter. Richins *et al.* does not teach or suggest that there was any promoter which was analogous to CaMV 35S in the FMV genome, in position, structure or

function. Based on Richins *et al.* it would not have been obvious to express genes from any particular region of the FMV genome as "yet another strong viral promoter" with a reasonable expectation of success.

As to the issue of position, Richins *et al.* does disclose the entire sequence of the DxS adapted strain of FMV, and compares open reading frames and intergenic sequences, finding some to be analogous to those found in the genomic organization of CaMV. A possible TATA location is disclosed as being within an intergenic sequence, in a location near the TATA location of the 35S promoter of CaMV.

While obviousness does not require absolute predictability of success, at least some is required. *In re Whiton* (CCPA 1970) 402 F.2d 1082; *In re Rinehart* (CCPA 1976) 531 F.2d 1048.

Richins *et al.* clearly state that the suggested location of a FMV promoter in the large intergenic region was a subjective choice, and that other TATA-like sequences are observed in this region (page 8464, second paragraph). Moreover, the homology to CaMV sequences noted by the authors (Figure 5, page 8460) is most prominent in a region downstream of the 34S FMV promoter. In fact, the open reading from (ORF) of gene VI is noted as being the least conserved region among the sequences of those caulimoviruses which were examined (Richins *et al.*, bottom of 8458). Nevertheless, the 5' upstream sequences that Applicants

determined to be important to the strength of the 34S FMV promoter lie precisely within this poorly conserved region.

Thus, the prior art in this case fails the initial inquiry of "obviousness" under §103 in that "something in the prior art as a whole must suggest the desirability, and thus the obviousness, of making the combination." *Uniroyal. Inc. v. Rudkin-Wiley Corp.*, 837 F.2d 1044, 1051-52 (Fed. Cir. 1988), *cert. denied*, 109 S.Ct. 75 (1988), *on remand*, 13 USPQ2d 1192 (D. Conn. 1989). *Alco Standard Corp. v. Tennessee Valley Authority*, 808 F.2d 1490, 1498 (Fed. Cir. 1986), *cert. dismissed*, 108 S.Ct. 26 (1987). As previously noted, Richins *et al.* analogizes certain structure between the FMV and CaMV genomes, not promoters, and the "34S" terminology is not in fact used by the authors of Richins *et al.* (it was coined by applicants). Richins *et al.* contains a sequence comparison, not a teaching regarding a particular region of the FMV genome which would be analogous in function with the CaMV 35S promoter, and Richins *et al.* never identify the particular region utilized by Applicants as the 34S promoter. No FMV promoter could be characterized as "yet another strong viral promoter" (page 2 of Final Office Action) until a particular region was tested and found, in fact, to be both a promoter and a strong promoter.

In her declaration (in Applicants May 17, 1993 response), Dr. Sanger notes that only the 35S CaMV plant viral promoter was characterized and well understood at the time of the present invention. Caulimoviruse are unique double-stranded DNA plant viruses. Where, as in this case, there is only a first well

characterized system, a simple comparison of sequences could not render obvious the location, function or important structure of regions in a second. As evidence that one can not, from a single example, extrapolate conclusions about promoters to other caulimovirus strains, Applicants have previously submitted, and now refer to, Hasegawa *et al.* (*Nucl. Acids Res.* (1989) *17*:9993-10013), which describe promoter activity in the soybean chlorotic mottle virus (SoyCMV) from a region IV upstream fragment. No such activity has been reported for other caulimoviruses, even though "promoter-like signals" are present at this location in CaMV.

It is the duty of the examiner to explain why a combination of the reference teachings is proper (*Ex parte Skinner*, 2 USPQ2d 1788, 1790 (PTO Bd. App. 1986)), by demonstrating that the references expressly or impliedly suggest the claimed combination or by presenting a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references. The Patent Office has repeatedly characterized the prior art as equating CaMV and FMV regions as analogous in location, function and activity. In fact, the prior art does not suggest any specific region for the FMV promoter, nor teach anything with regard to its function.

From superficial resemblances noted between the CaMV genome and that of the FMV by the prior art references, a

promoter of the type claimed by Applicants was at best only "obvious to try".

> The admonition that "obvious to try" is not the standard under §103 has been directed mainly at two kinds of error. In some cases, [w]hat would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. In others, what was "obvious to try" was to explore a new technology or a general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it.

In re O'Farrell 7 U.S.P.Q. 2d at 1681 (Fed. Cir. 1988).

In fact, while there is some speculation in Richins *et al.* regarding possible FMV promoter locations, based on comparisons with the CaMV genome and location of putative TATA boxes, and identification of regions of conserved sequence among viruses, far from leading one expectantly to the claimed promoter, Richins *et al.* focuses on sequences 3', or downstream, of the TATA location (pages 8460-8461). Applicants found little or no contribution to promoter activity from such downstream sequences.

Thus, the similarities noted by Richins *et al.* between the 35S promoter sequence of CaMV and the putative TATA teach away from, as much as suggest anything meaningful regarding Applicants 34S promoter. Only in hindsight, with Applicants invention in hand, might it appear obvious that a given region of the genomic sequence provided by Richins *et al.* should function as a promoter, or that a region could be substituted for an analogous

region of CaMV. It is inappropriate, however, to use the invention as a template to piece together the teachings of the prior art. *In re Fritch*, 972 F. 2d 1260, 1266 (Fed. Cir. 1992). "It is impermissible ... simply to engage in a hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps." *In re Gorman*, 933 F. 2d 982, 987 (Fed. Cir. 1991). Unlike Applicants, the authors of Richins *et al.* did not test FMV sequences in constructs to determine the actual location and extent and strength of any promoter. It is Applicants who first characterized the promoter of FMV and designated it as "34S". Given the simple comparison of the FMV genomic sequence to the genomic sequence of CaMV in Richins *et al.*, with no results of tests, or even identification of what regions should be tested for promoter activity, Richins *et al.* would have at best led one skilled in the art to speculate as to the location of any functions in the FMV genome.

In view of the above, Applicants submit that the rejection under 35 U.S.C. §103 over the combination of Shah *et al.* and Sanders *et al.* taken with Richins *et al.* or Gowda *et al.* or Wu *et al.* or Goldberg *et al.* be reversed.

Issue 4

Claims 20, 22-28, 30, 33-36 and 43 are rejected under 35 U.S.C. 103 over the combination of Shah *et al.* and Sanders *et al.* taken with Richins *et al.* and Shepherd *et al.*, as applied in the last Office Action and as repeated. Shah *et al.*, Sanders *et al.*

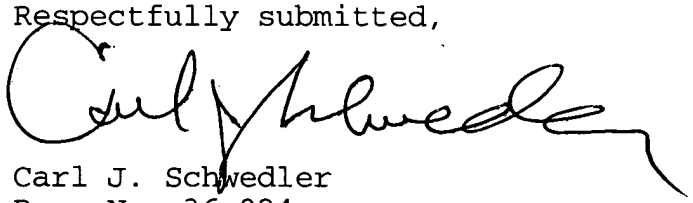
and Richins *et al.* are discussed more fully above. These references do not provide one with the instantly claimed invention.

Shepherd *et al.* teaches that FMV is amenable to cloning manipulation, as Shepherd *et al.* provides a restriction map for the virus. The Patent Office states that Shepherd *et al.* echoes the disclosure in Richins *et al.* that the "34S promoter" of FMV was analogous to CaMV 35S in position, structure, function and was expected to have strong expression characteristics. The Patent Office further states that Shepherd *et al.* compared CaMV and FMV promoters.

In light of the fact that Shepherd *et al.* does not characterize any particular region as a "promoter" regions, does not use the term "34S promoter", in fact discloses no FMV sequence at all, and reports no tests of FMV promoter activity, a comparison of <u>promoters</u> would have been impossible from Shepherd *et al.* Shepherd *et al.* never identifies Applicants' 34S promoter at all, other than a suggestion of a suspected correlation to the gene VI region of CaMV, including intergenic regions. As is the case for the Richins *et al.* reference, the genome is noted as being not particularly homologous to CaMV at this region (page 1672, second column in Shepherd *et al.*). Shepherd *et al.* offers nothing which would lead one ordinarily skilled in the art to any promoter from the FMV genome, let alone the claimed 34S promoter of FMV.

For all of the above reasons, reversal by Board of Patent Appeals and Interferences of the Issue 4 rejection of the claims is respectfully requested.

Respectfully submitted,



Carl J. Schwedler
Reg. No. 36,924

CALGENE, INC.
1920 Fifth Street
Davis, CA 95616
(~~916~~) 753-6313
530

APPENDIX

20. A recombinant DNA construct capable of transcription in a plant cell comprising in the 5' to 3' direction of transcription as operably joined components, a figwort mosaic virus 34S promoter, a DNA sequence of interest heterologous to said promoter and a transcript termination region functional in a plant cell.

22. The recombinant DNA construct of Claim 20 wherein said transcript termination region is from the 3' flanking region of the mannopine synthase gene.

23. The recombinant DNA construct of Claim 20 wherein said figwort mosaic virus 34S promoter comprises a TATA box having the sequence TATTTAA.

24. The recombinant DNA construct of Claim 20 wherein said figwort mosaic virus 34S promoter comprises at least 196bp 5' of the TATTTAA at nucleotides 894 to 900 of Figure 4.

25. The recombinant DNA construct of Claim 20 wherein said figwort mosaic virus 34S promoter comprises at least 362bp 5' of the TATTTAA at nucleotides 894 to 900 of Figure 4.

26. The recombinant DNA construct of Claim 20 wherein said figwort mosaic virus promoter comprises at least 892bp 5' of the TATTTAA at nucleotides 894 to 900 of Figure 4.

27. The recombinant DNA construct of Claim 20 wherein said DNA sequence of interest is a structural gene.

28. The recombinant DNA construct of Claim 20 wherein said DNA sequence of interest is an anti-sense DNA sequence.

30. The recombinant DNA cassette of Claim 43 wherein said DNA sequence of interest joined to said CaMV 35S promoter is different from said DNA sequence of interest joined to said figwort mosaic virus promoter.

33. The recombinant DNA construct of Claim 20 further comprising a 5' untranslated leader sequence.

34. The recombinant DNA construct of Claim 33, wherein said 5' untranslated sequence is from a figwort mosaic virus 34S promoter.

35. A plant cell comprising a recombinant DNA construct of any one of Claims 20, 22-28, 30, 33-34 and 43.

36. A plant comprising a recombinant DNA construct of any one of Claims 20, 22-28, 30, 33-34 and 43.

43. A DNA cassette for plant genetic engineering applications, wherein said DNA cassette comprises a recombinant DNA construct of Claim 20, and a second recombinant DNA construct comprising as operably joined components in the 5' to 3' direction of transcription, a CaMV 35S promoter, a DNA sequence of interest and a transcript termination region functional in a plant cell.